

## PATENT COOPERATION TREATY

#6 attachment  
09/87532/PLM  
JWt  
MKX

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:  
FISH & RICHARDSON P.C.  
Attn. Myers, Louis  
225 Franklin Street  
Boston, Mass 02110-2804  
UNITED STATES OF AMERICA

RECEIVED

MAR 19 2002

FISH & RICHARDSON, P.C.  
BOSTON OFFICE

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

Applicant's or agent's file reference <b>10448-061W01</b>	Date of mailing (day/month/year) <b>12/03/2002</b>
International application No. <b>PCT/US 01/ 18340</b>	International filing date (day/month/year) <b>06/06/2001</b>
Applicant <b>MILLENNIUM PHARMACEUTICALS, INC.</b>	

## 1. This International Searching Authority

- (i) considers that there are 3 (number of) inventions claimed in the international application covered by the claims indicated ~~below~~ on the extra sheet:

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated ~~below~~ on the extra sheet:

Classified by Office Secretary  
Date: 4-26-02  
Examiner: FA (over) 6-12-02  
Inspector: RS

Docketed By Practice Systems

See Invitation 4/24/02  
PTA (061001) 6/12/02Initials: CHS  
Record: [ ]

- (ii) ☒ has carried out a partial international search (see Annex) on those parts of the international application which relate to the invention first mentioned in claims Nos.:  
**1-30 (all partially)**

- (iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid


## 2. The applicant is hereby invited, within the time limit indicated above, to pay the amount indicated below:

EUR 945,00 x 2 = EUR 1.890,00  
Fee per additional invention      number of additional inventions      total amount of additional fees

Or, \_\_\_\_\_ x \_\_\_\_\_ = \_\_\_\_\_

The applicant is informed that, according to Rule 40.2(c), the payment of any additional fee may be made under protest, i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. ☒ Claim(s) Nos. further info have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer <b>Henriëtte Huysing-Solles</b>
--	---

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-30 (all partially)

An isolated nucleic acid molecule which is at least 95% identical to SEQ ID NO:1 or 3, or comprising a fragment of at least 1750 nucleotides of SEQ ID NO:1 or 3, or which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or a fragment comprising at least 580 contiguous amino acids of SEQ ID NO:2 or a naturally occurring allelic variant thereof. A vector and a host cell comprising said nucleic acid molecule. An isolated polypeptide encoded by said nucleic acid molecule and a method for producing it. An antibody binding to said polypeptide. Methods for detecting said polypeptide and said nucleic acid molecule. A method for identifying a compound binding to said polypeptide. A method for modulating the activity of said polypeptide comprising contacting with a compound binding to said polypeptide. A method for identifying a compound which modulates the activity of said polypeptide. A method of treating or preventing an ion flux-related disorder comprising administering an agent modulating the activity or expression of said polypeptide or nucleic acid. A method for identifying an agent that modulates the activity or expression of said polypeptide or nucleic acid.

2. Claims: 1-7,16-18 (all partially); 31 (completely)

An isolated nucleic acid molecule which is at least 95% identical to SEQ ID NO:4, or comprising a fragment of at least 2980 nucleotides of SEQ ID NO:4. A vector and a host cell comprising said nucleic acid molecule. A method for detecting said nucleic acid molecule. An antibody binding to an extracellular domain of the polypeptide of SEQ ID NO:5.

3. Claims: 1-30 (all partially)

An isolated nucleic acid molecule which is at least 90% identical to SEQ ID NO:7, or comprising a fragment of at least 300 nucleotides of SEQ ID NO:7, or which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:8 or a fragment comprising at least 80 contiguous amino acids of SEQ ID NO:8 or a naturally occurring allelic variant thereof. A vector and a host cell comprising said nucleic acid molecule. An isolated polypeptide encoded by said nucleic acid molecule and a method for producing it. An antibody binding to said polypeptide. Methods for detecting said polypeptide and said nucleic acid molecule. A method for identifying a compound binding to said polypeptide. A method for modulating the activity of said polypeptide comprising contacting with a compound binding to said polypeptide. A method for identifying a compound which modulates the activity of said polypeptide. A method of treating or preventing an ion flux-related disorder

comprising administering an agent modulating the activity or expression of said polypeptide or nucleic acid. A method for identifying an agent that modulates the activity or expression of said polypeptide or nucleic acid.

#### Motivation of the Objection against Unity

---

Human potassium channels and their encoding polynucleotides are well known in the prior art. E.g., W09811139 and W09903882 respectively disclose the human potassium channels hSK1, hSK2 and hSK3, and the human potassium channel hKCa4, as well as encoding polynucleotides and uses.

Therefor, in the light of the prior art, the problem underlying this application can be defined as the provision of further human potassium channel proteins and polynucleotides encoding them. The solutions as disclosed and claimed (or claimed partially) can be summarized as each of the three claimed proteins SEQ ID NOs 2 ("52906"), 5 ("33408") and 8 ("12189") and/or the corresponding nucleotide sequences of SEQ ID NOs 1 and 3, 4 and 6, and 7 and 9, respectively, and their uses.

In view of the fact that human potassium channels and polynucleotides encoding them have already been disclosed in the prior art, due to the essential differences in primary structure of the polypeptides and the encoding polynucleotides, and due to the fact that no other technical features can be distinguished which, in the light of the prior art, could be regarded as special technical feature common to these solutions, the ISA is of the opinion that there is no single inventive concept underlying the plurality of claimed inventions of the present application in the sense of Rule 13.1 PCT. Consequently there is a lack of unity and different inventions, not belonging to a common inventive concept are formulated as the different subjects on the communication pursuant to Art. 17(3)(a), PCT.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

Continuation of Box 3.

Although claims 21 and 23-25 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

-----

Further defect(s) under Article 17(2)(a):

Continuation of Box 3.

Present claims 15, 18, 21 and 23-25 relate to a compound/agent defined by reference to a desirable characteristic or property, namely binding or hybridizing to or modulating the activity or expression of a 52906 polypeptide or nucleic acid. The claims cover all compounds/agents having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds/agents. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound/agent by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to antibody and antisense molecules.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:  
see 'Invitation to pay additional fees'
2. This communication is not the international search report which will be established according to Article 18 and Rule 43.
3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.
4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 11139 A (UNIV OREGON HEALTH SCIENCES ;ADELMAN JOHN P (US); BOND CHRIS T (US) 19 March 1998 (1998-03-19) Note: 99.8% nt seq identity of SEQ ID NO:21 with SEQ ID NO:3 in 1740 nt overlap (1-1740:805-2544), 99.8% aa seq identity of SEQ ID NO:19 with SEQ ID NO:2 in 579 aa overlap (1-579:269-847) the whole document page 5, line 14 -page 12, line 3 page 26, line 12 -page 29, line 30 page 106-108 page 110-111 claims 2-4,12-14,21,22,24-48 ---	1-30
Y	DATABASE EM_EST 'Online! EMBL; ID AI271784, AC AI271784, 19 November 1998 (1998-11-19) NCI-CGAP: "qj82f08.x1 NCI_CGAP_Kid3 Homo sapiens cDNA clone IMAGE:1865991 3' similar to contains element TAR1 repetitive element ;, mRNA sequence" XP002191022 Note: 100.0% nt seq identity with SEQ ID NO:3 in 413 nt overlap (1-413:818-406) the whole document --- -/--	1-30

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JÄGER H ET AL.: "SK2 encodes the apamin-sensitive Ca <sup>2+</sup> -activated K <sup>+</sup> channels in the human leukemic T cell line, Jurkat." FEBS LETTERS, vol. 469, no. 2-3, 10 March 2000 (2000-03-10), pages 196-202, XP002191020 ISSN: 0014-5793 abstract page 201, left-hand column, line 1-17 page 201, right-hand column, line 23-60 ---	1-30
A	WO 99 47923 A (MACKINNON RODERICK ;UNIV ROCKEFELLER (US)) 23 September 1999 (1999-09-23) the whole document ---	19-30
A	WO 99 03882 A (ZENECA LTD) 28 January 1999 (1999-01-28) the whole document ---	1-30
P,A	DESAI R ET AL.: "Ca <sup>2+</sup> -activated K <sup>+</sup> channels in human leukemic Jurkat T cells: Molecular cloning, biochemical and functional characterization." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 275, no. 51, 22 December 2000 (2000-12-22), pages 39954-39963, XP002191021 ISSN: 0021-9258 Note: 99.7% aa seq identity of hSK2 (KCN2) with SEQ ID NO:2 in 579 aa overlap (1-579:269-847) the whole document -----	1-30

**Patent Family Annex**  
Information on patent family members

International Application No  
**PCT/US 01/18340**

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9811139	A	19-03-1998	AU 726158 B2	02-11-2000
			AU 4266097 A	02-04-1998
			EP 0948542 A1	13-10-1999
			JP 2000514310 T	31-10-2000
			WO 9811139 A1	19-03-1998
WO 9947923	A	23-09-1999	AU 3198899 A	11-10-1999
			EP 1062508 A1	27-12-2000
			WO 9947923 A2	23-09-1999
WO 9903882	A	28-01-1999	AU 8348498 A	10-02-1999
			EP 1012281 A2	28-06-2000
			WO 9903882 A2	28-01-1999
			JP 2001520524 T	30-10-2001